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09/903,395	07/10/2001	Keith D. Allen	R-653	9465

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,395	ALLEN, KEITH D.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11-10-4*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,39 and 41-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,39 and 41-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-37 and 40 have been canceled. Claims 41-47 have been added. Claims 38, 39 and 41-47 are pending and are under consideration in the instant office action.

Specification

The application numbers throughout the specification will require updating as necessary.

Claim Rejections - 35 USC § 101

Claims 38 and 39 remain rejected and claims 41-47 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility for reasons of record.

> REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS repeated from http://www.uspto.gov/web/menu/utility.pdf
>
> "Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.
>
> "Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial

utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

(Page 5-7 of utility guidelines).

A "well-known utility" is a specific, substantial and credible utility which is well know, immediately apparent, or implied by the specification's disclosure of the properties of the material, alone or taken with the knowledge of one skilled in the art. Neither a "well-established utility" nor a "specific utility" applies to any utility that one can dream up for an invention or a utility that would apply to virtually every member of a general class of materials, such as proteins or DNA.

(Paragraph bridging pg 32-33 of utility guidelines).

Claims 38, 39 and 41-46 are directed toward a transgenic mouse whose genome has a null MC3-R allele, said allele comprising with the nucleic acid sequence of SEQ ID NO:1, said null allele comprising exogenous DNA, said exogenous DNA comprising a gene encoding a visible marker, wherein in a male transgenic mouse said gene is capable of expression in the testis.

The specification teaches expression analysis of the mice on pg 53-54.

The mice claimed and described in the expression analysis study do not have a specific or substantial utility. The specification does not teach the structure of the knockout construct so that one of skill could determine what promoter is driving expression of the LacZ gene. Specifically, it cannot be determined that the LacZ gene is linked to the MC3-R gene promoter. If the LacZ gene is operably linked to the MC3-R promoter, the specification does not teach how to use a male mouse that expresses LacZ in its testes to determine the function of MC3-R. It is not readily apparent that the expression pattern data is statistically significant because the number of mice tested is not disclosed. And finally, the expression analysis does not provide the function of the MC3-R gene. Significant "further experimentation" would be required to use the expression analysis to determine the function of the MC3-R gene. Specifically, it must be determined which cells of the testes express MC3-R and what the function of MC3-R is within those cells of the testes. It is unclear if MC3-R is linked to hormone production, sperm production or temperature regulation. As such, male mice with a disruption in the MC3-R gene comprising SEQ ID NO:1, capable of expressing a visible marker in the testes as claimed do not have a specific or substantial utility.

The specification teaches making MC3-R -/- mice having only one kidney (pg 53, line 5-10). The specification teaches male MC3-R -/- mice were passive and hypoactive while females were not (pg 54, lines 13-15).

The mice claimed and described in the specification do not have a specific or substantial utility. The specification suggests using the mice as a model of disease, specifically as a model for behavioral abnormalities, such as neurological,

neuropsychological, psychotic phenotypes (pg 19-21; pg 21, lines 6-10). The specification does not disclose that behavioral abnormalities, specifically neurological, neuropsychological or psychotic disease found in humans, are linked to a disruption in MC3-R. The specification does not provide any use for a mouse with one kidney or a passive/hypoactive male, how such a mouse correlates to any disease, or that a disruption in MC3-R is found in hypoactive humans. Passive and hypoactive mice are not specific to any disease and are not linked to a disruption in an MC3-R gene in humans. The results of the behavioral tests are also not statistically significant because the number of mice tested is not disclosed. Thus, the asserted utility of using the mice as a model of disease is not a specific, substantial or credible utility.

Since the time of filing, Watanobe (Neuroendrocrinology, 2003, Vol. 78, pg 331-338) suspected MC3-R played a role in leptin-stimulated or spontaneous GH secretion. Watanobe was wrong ("neither MC4-R or MC3-R is involved in leptin-stimulated or spontaneous GH secretion" at the end of the abstract). Thus, the mouse claimed may be used for scientific research but may not provide the function of the MC3R gene.

Rached (Biochimica et Biophysica Acta, 2004, Vol. 1689, pg 229-234) taught MC3R was expressed primarily in the brain of mammals and was linked to obesity (see abstract). Applicants tested expression in the brain but did not teach MC3R was expressed in the brain (pg 53). Applicants did not contemplate the MC3R gene was linked to obesity. Therefore, the specification does not provide a substantial, specific or credible utility for a mouse with a disruption in

the MC3R gene. Thus, the specification did not teach the elements essential to use the mouse claimed as a model for obesity in humans.

Claim 47 is directed toward identifying agents capable of modulating activity of MC3-R gene or MC3-R gene expression product by administering a putative agent to the transgenic mouse of claim 38 and a wild-type mouse, and comparing the physiological responses of the mice, wherein the physiological response is a change in passive behavior. The specification suggests using the mice to identify agents that ameliorate a phenotype (pg 20, line 4-5). Using the mice to identify agents capable of altering a phenotype would require further research and is not a "substantial utility" or "specific utility" because the mouse may not be capable of identifying agents capable of treating disease. Bowery (Pharm. Rev., 2002, Vol. 54, pg 247-264) taught,

> "no unique pharmacological or functional properties have been assigned to either subunit or the variants" of $GABA_B$. "The emergence of high-affinity antagonists for $GABA_B$ receptors has enabled a synaptic role to be established. However, than antagonists have generally failed to establish the existence of pharmacologically distinct receptor types within the $GABA_B$ receptor class. The advent of $GABA_{B1}$ knockout mice has also failed to provide support for multiple receptor types" (pg 247, col. 2, line 4 on).

Thus, knockout mice may be used to identify agents that bind to the knocked out gene ($GABA_B$ in the case of Bowery or GPCR-like protein in the instant application), but the agent may not treat disease or ameliorate any symptom of disease. Further research would be required to determine how to use such an

agent identified using the mouse, which is not a "substantial utility" (see Utility Guidelines for examples of things that do not have "substantial utility" "C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility"). Using the mice to identify agents capable of altering a phenotype is also not a "specific utility" because the agent may be affecting other proteins in the pathway and not the MC3-R protein itself. Using the mice to identify agents capable of altering a phenotype is also not a "specific utility" because the agent may be found using wild-type mice. Furthermore, the specification does not identify any such agents using the mice. Therefore, using the mice to identify agents that alter the increased sensitivity to pain is not a specific, substantial or credible utility.

It is interesting to note that since the time of filing Barb (J. Endocrinology, 2004, Vol. 181, pg 39-52) administered agonists and antagonists of MC3R to wild-type pigs to assay in an attempt to determine the role of MC3R in regulating appetite, energy homeostasis and neuroendocrine function. The specification did not teach the agonists or antagonists, which would have required significant further research to identify in and of themselves. The specification did not teach the MC3R gene was involved in regulating appetite, energy homeostasis or neuroendocrine function as suggested by Barb. Most importantly, Barb emphasizes the examiner's position that administering compounds to a mouse to determine the function of the MC3-R gene as generically suggested in the specification can be done using a wild-type mouse. The knockout mouse

described in the specification provides no greater utility over a wild-type mouse for the assays generically described in the specification.

The specification suggests using the mice to identify agents that affect MC3-R function (pg 20, lines 19-21). The mouse claimed cannot be used to identify agents that act on MC3-R because the mice do not express MC3-R.

It was "well-known" in the scientific community at the time of filing to knock out a gene in a mouse in an attempt to determine its function; however, it was also "well-known" that the mouse may only provide clues to the function of the gene and that the mouse may not be capable of determining the function of the gene. While the mouse may have "scientific utility," "scientific utility" is not the same as "patentable utility" or a "well-established" utility.

The utility guidelines specifically state that further research is not a "substantial utility":

> [T]he following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

In this case, further study of mice would have been required to determine how to use the mouse of applicants' invention as a model of disease. While applicants determined lacZ expression was detectable in the testis, extensive study would be required to determine the function of the MC3-R gene in the

testis. The overall phenotype of the applicants' mice does not correlate to any disorder; therefore, further study would be required to determine how to use the mice to study a disorder. Thus, using the mice claimed for further research is not a "substantial utility."

Using the mice to identify the function of the MC3-R gene is not a "substantial utility" or "specific utility" because the phenotype may be caused by other proteins compensating for the deleted MC3-R gene. Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). Thus, knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Using mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype may be a result of other compensating proteins and not the knocked out gene.

The function of the MC3-R gene may not be found by studying the knockout mouse claimed. Mombereau (Neuropsychopharmacology, 2004, Vol. 29, pg 1050-

1062) used knockout mice that had increased anxiety further study to determine the function of $GABA_B$ receptor. Mombereau did not teach how to use mice with decreased anxiety as claimed. In addition, Mombereau did not determine the function of the $GABA_B$ receptor. Mombereau administered compounds known to antagonize $GABA_B$ receptor (found in *in vitro* assays, not in the mice) to the mice. Mombereau concluded that the mice merely confirmed $GABA_B$ was involved in a molecular pathway relevant for the manifestation of anxiety or depression. Mombereau did not determine the function of $GABA_B$ receptor using the $GABA_B$ -/- mice. Mombereau concludes "we acknowledge both the inherent difficulties and the caution needed in the interpretation of behavioral analysis of genetically modified mice such as the $GABA_B(1)$ -/- mice, which have overt behavioral disturbances, in more defined tests relevant to psychopathology. Nonetheless, the current data show that even such mice can still be utilized to give important indicators of the role of a given protein, in this case the $GABA_B$ receptor, in a molecular pathway relevant for the manifestation of anxiety or depression. These assertions can then be confirmed more parametrically using appropriate pharmacological activators and antagonists as we have done using novel $GABA_B$ receptor positive modulators and antagonists" (¶ bridging pg 1059-1060). Mombereau used the antagonists to confirm the "antidepressant-like phenotype of $GABA_B$ -/- mice pharmacologically (pg 1059, col. 1, 2nd full ¶, line 1-4). Therefore, using a MC3-R -/- mouse to merely obtain clues of the role of MC3-R in vivo is not a specific or substantial utility because it is generic and does not necessarily result in determining the function of MC3-R.

Overall, the mice claimed do not have a "well-established utility" because using the mice for further research (to determine how to use the mouse as a model of non-disclosed disease, to determine the function of the gene or to identify agents capable of altering a phenotype) is not a "specific utility" or "substantial utility."

Applicants argue that one of skill would have recognized that the mouse has a well-established utility for defining the function and role of the disrupted gene, i.e. a tool in studying gene function (pg 7, 2nd full ¶ of response filed 11-8-04). Applicants cite MPEP 2701 II(A)(3). Applicants cite an NIH report from 2004, Austin (Nature Genetics, 2004, Vol. 36, No. 9, pg 921-24), Genes VII (Lewin, Oxford University Press, 2000), Crawley (2000, What's wrong with my mouse, Behavioral phenotyping of transgenic and knockout mice, Wiley-Liss) and Crabbe (Science, 1999, Vol. 284, pg 1670-1672), which state knockout mice can be used to determine the function of genes. Applicants' arguments are not persuasive. MPEP 2701 II(A)(3) states:

> If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible. (underlining added for emphasis)

Thus, the MPEP states a well-established utility must be specific, substantial and credible. All of the cited references simply state that knockout mice can be used to study the function of the disrupted gene. None of the cited references state the function of the gene will be determined using a knockout mouse. As a whole, the cited

references support the examiners position that knockout mice are simply used for "further research" to provide clues as to the function of the gene.

In this case, using MC3-R -/- mice to determine the function of the MC3-R gene rises merely to the level of a scientific utility, but does not rise to the level of a specific, substantial and credible utility. Significant further research would be required to determine the function of the MC3-R gene using only the expression analysis data of the MC3-R -/- mice described in the specification. Specifically, it must be determined which cells of testes express MC3-R, what the function of MC3-R is within those cells of the testes and how MC3-R may be linked to passive behaviour/hypoactivity. Numerous examples since the time of filing have done such further experimentation in knockout mice, including administering known antagonists of the knocked out gene to the knockout and wild-type mice, and still have not determined the function of the knocked out gene (Bowery, Olsen and Mombereau, all cited above). As such, male mice with a disruption in SEQ ID NO:1 (the MC3-R gene) that are merely characterized as expressing a marker protein in the testes, passive and hypoactive do not have a "well-known" utility because the mice do not have a specific or substantial utility.

Male mice with a disruption in SEQ ID NO:1 (the MC3-R gene) that express a marker protein in the testes, are passive and hypoactive do not compare to "gas chromatographs, screening assays and nucleotide sequencing techniques" as argued in the middle of pg 10 of the response because the mice may not reveal the function of the MC3-R gene. In the case of gas chromatographs, assays and lab screening techniques, the products apply to numerous materials and provide specific data that

amount of a chemical in a product, the amount of a protein, the presence of a gene, the nucleotide sequence of a gene, etc. In this case, the mouse is capable of providing gene expression analysis data, but the gene expression analysis data does not provide the function of the gene. The mouse may provide a clue that the MC3-R gene correlates to male passive behavior, but the phenotype may be a result of other genes compensating for the disruption of the MC3-R gene. If the passive/hypoactive behavior is a result of the MC3-R disruption, a mouse with passive hypoactive behavior caused by a disruption in the MC3-R gene still does not provide the function of the MC3-R gene. Therefore, using the mice to determine the function of the MC3-R gene is not a well-established utility that is specific or substantial.

Applicants argue the mice have been ordered by at least four pharmaceutical companies; therefore, applicants conclude that those of skill would recognize the utility of the mice (pg 10 of arguments). Applicants' argument is not persuasive. Sales may be evidence to overcome a 103 obviousness rejection, but there is no case law that establishes that "sales" are evidence of patentable utility. Evidence of sales is not evidence the mice have a "well-established" utility or a "specific utility" or a "credible utility."

Applicants argue the motivational statement in the 103 rejection shows that those of skill in the art at the time of filing wanted to disrupt genes in mice to determine the function of the genes (¶ bridging pg 10-11). Applicants' argument is not persuasive. Motivation to disrupt a gene in a mouse to determine the function of the genes clearly existed at the time of filing. The desire to determine

the function of MC3-R in the art at the time of filing did not guarantee a MC3-R knockout mouse would reveal the function of the MC3-R gene or a MC3-R knockout mouse was a model of disease.

Applicants cite en re Brana and state the PTO has the initial burden of challenging the asserted utility in the disclosure (pg 11-12 of response). Applicants argue that contrary to the product in En re Brenner, whose sole 'utility' consisted of its potential role as an object of use-testing, the mouse claimed can be used to determine the function of SEQ ID NO:1. Applicants' arguments are not persuasive. *In re Schoenwald*, 22 USPQ2d 1671 (CA FC 1992) indicated that a product known in the art did not necessarily have patentable utility. The examiner has challenged all of the asserted utilities in the disclosure and has challenged what applicants consider "well-established" utilities. The mouse claimed might only provide a clue to a pathway in which SEQ ID NO:1 is involved. This is not a specific utility because results from the tests only indicate SEQ ID NO:1 is involved in a pathway relating to decreased anxiety. The phenotype provides only a clue that SEQ ID NO:1 is generically involved in a signal transduction pathway having a number of proteins. Using the mouse to determine the function of SEQ ID NO:1 is not credible or substantial because the function of SEQ ID NO:1 may never be found using the MC3-R mouse claimed. Assuming further study of the mouse will elucidate the function of SEQ ID NO:1, the amount of research required to do so would be significant. The specification does not guide those of skill in any particular

direction so that one of skill could simply perform an assay to determine the function of SEQ ID NO:1.

Applicants cite Doetschman (Lab. Animal Sci. 1999; Vol. 49, pg 137-143), which taught knockout phenotypes provide accurate information concerning gene function (middle of pg 13). Applicants' argument is not persuasive. Doetschman taught that the phenotype may be caused by the mixed background of the knockout mice and not be caused by the knockout (¶ bridging pg 28-29). Doetschman does not teach that every mouse with a disruption will reveal the function of the disrupted gene. Using a knockout mouse to "provide information about the function of a gene" as described by Doetschman is not the same as providing the function of the gene as asserted by applicants. The knockout mice described by Doetschman merely provide clues as to the disrupted gene's function. Significant further investigation would be required to determine the function of a gene using any mouse described by Doetschman.

Claim Rejections - 35 USC § 112

Enablement

Claims 38 and 39 remain rejected and claims 41-47 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set

forth above, one skilled in the art clearly would not know how to use mice having a disruption in an MC3-R gene as claimed.

Applicants' arguments are those made in the utility rejection and have been addressed above.

New Matter

Claims 38 and 39 as amended and new claims 41-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "null allele" in claim 38 is new matter because the phrase does not have support in the specification as originally filed on pg 8, lines 25-28; pg 19, line 19, through pg 21, line 10, Example 1, the Figures, or the claims as originally filed as asserted by applicants.

The specification as originally filed does not contemplate a null allele comprising exogenous DNA encoding any visible marker capable of expression in the testis as newly amended in claim 38. The phrase does not have support in the specification as originally filed on pg 8, lines 25-28; pg 19, line 19, through pg 21, line 10, Example 1, the Figures, or the claims as originally filed as asserted by applicants. The specification only contemplates inserting the LacZ-neo cassette into the MC3-R gene as described in

Fig. 2B. (It is noted that the specification does not completely describe the structure of the knockout construct by describing where the LacZ-neo cassette was inserted into the MC3-R gene, what promoter was used to drive expression of LacZ or neo or how much of the MC3-R gene remained in the construct.

Identifying agents that modulate "activity or MC3-R gene or MC3-R gene product" as broadly claimed in new claim 47 was not contemplated in the specification as originally filed. The phrase does not have support in the specification as originally filed on pg 8, lines 25-28; pg 19, line 19, through pg 21, line 10, Example 1, the Figures, or the claims as originally filed as asserted by applicants.

The specification as originally filed did not teach how to compare "a change in passive" of a transgenic mouse with a control mouse as newly claimed in claim 47. The specification did not teach how to compare "changes." The phrase does not have support in the specification as originally filed on pg 8, lines 25-28; pg 19, line 19, through pg 21, line 10, Example 1, the Figures, or the claims as originally filed as asserted by applicants.

The specification as originally filed did not contemplate identifying agents that modulate MC3-R gene activity by determining "a difference in the physiological response between the transgenic mouse and the control mouse is an indication that the agent is capable of modulating activity of the MC3-R gene or a MC3-R gene product" as newly claimed in claim 47. The phrase does not have support in the specification as originally filed on pg 8, lines 25-28; pg 19, line 19, through pg 21, line 10, Example 1, the Figures, or the claims as originally filed as asserted by applicants.

35 U.S.C. 112, second paragraph

Claims 38 and 39 as newly amended and new claims 41-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 as amended is indefinite because a mouse cannot have a null MC3-R allele, wherein the allele comprises SEQ ID NO:1. As written it appears as though applicants are claiming the mouse has a disruption of the MC3-R allele, SEQ ID NO:1, while at the same time the null allele comprises SEQ ID NO:1. The allele of the mouse being claimed cannot have both a null MC3-R allele and an allele comprising SEQ ID NO:1.

The phrase "null MC3-R allele" in claim 38 is indefinite. It is unclear if the phrase is limited to a mouse without any of the MC3-R gene, or if the phrase encompasses a mouse without any of the coding region of the MC3-R gene, or a mouse with a disruption in the MC3-R gene, wherein said disruption does not allow production of functional MC3-R protein, or a mouse with a disruption in the MC3-R gene, wherein said disruption causes less than normal amounts of function MC3-R protein. The metes and bounds of what applicants consider "null" cannot be determined.

The step of comparing "a change in passive behavior" in claim 47 is indefinite. It is unclear if the knockout and control mice are tested before being given the agent and then again after being given the agent and the change for each is compared or if the knockout and control mice are tested after being given the agent and then tested and compared.

The phrase "wherein the physiological response is a change in passive behavior" is unclear. Passive behavior is a psychological behavior not a physiological behavior as claimed.

Claim Rejections - 35 USC § 102

Claims 38 and 39 remain rejected and claims 41-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Butler (Sept. 2000, Endocrinology, Vol. 141, pg 3518-3521) for reasons of record.

The effective filing date of claims 38, 39 and 41-47 is 10-26-00, the filing date of 60/243,958, which taught male homozygous mice were passive (pg 69, last 3 lines). Claims 38, 39 and 41-47 do not get priority to Provisional application 60/218,074, filed July 12, 2000, because '074 did not teach that the mouse with a disruption in SEQ ID NO:1 was passive as claimed.

Butler taught male mice with a homozygous disruption in the MC3-R gene had reduced energy expenditure as determined by reduced wheel running behavior (pg 3520, col. 1, last full ¶). Reduced wheel running is considered passive behavior as claimed. The mice taught by Butler inherently do not attempt to escape as claimed because they were made using the method described in the specification and have the same structure as the mice described in the specification, i.e. the MC3-R gene in Butler is SEQ ID NO:1 and the disruption of the MC3-R gene in Butler is the same disruption disclosed in the instant application. Therefore, the mouse of Butler inherently exhibit a

decrease in attempts to escape because it has the same structure disclosed in the instant application. The wheel is "a putative agent" and determining the amount or speed or running while on the wheel is equivalent to the "determining..." step in claim 40.

Applicants argue Butler cannot be used as prior art because Butler does not predate the original filing date of provisional application 60/218,074, filed July 12, 2000. applicants' argument is not persuasive. Claims 38, 39 and 41-47 do not get priority to Provisional application 60/218,074, filed July 12, 2000, because '074 did not teach that the mouse with a disruption in SEQ ID NO:1 was passive as claimed. Butler (Sept. 2000) is prior art because it predates the effective filing date of 60/243,958 (Oct. 26, 2000).

Claim Rejections - 35 USC § 103

Claims 38 and 39 remain rejected and claims 41-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butler (Sept. 2000, Endocrinology, Vol. 141, pg 3518-3521) in view of Desarnaud (1994, Biochem. J., Vol. 299, pg 367-373) for reasons of record.

The effective filing date of claims 38, 39 and 41-47 is 10-26-00, the filing date of 60/243,958. Claims 38, 39 and 41-47 do not get priority to Provisional application 60/218,074, filed July 12, 2000, because '074 did not teach that the mouse with a disruption in SEQ ID NO:1 was passive as claimed.

Butler taught male mice with a homozygous disruption in the MC3-R gene had reduced energy expenditure as determined by reduced wheel running behavior (pg 3520, col. 1, last full ¶). Reduced wheel running is considered passive behavior as claimed. The wheel is "a putative agent" and determining the amount or speed or running while on the wheel is equivalent to the "determining..." step in claim 47. Butler did not teach the MC3-R gene was SEQ ID NO:1 as claimed.

However, Desarnaud taught SEQ ID NO:1.

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to disrupt the MC3-R gene as taught by Butler, wherein the MC3-R gene had the nucleic acid sequence of SEQ ID NO:1 taught by Desarnaud. One of ordinary skill in the art at the time the invention was made would have been motivate to disrupt SEQ ID NO:1 taught by Desarnaud as the MC3-R gene taught by Butler because SEQ ID NO:1 is the MC3-R gene. One of ordinary skill in the art at the time the invention was made would have been motivate to determine if the MC3-R gene of Desarnaud had the same effect as the MC3-R gene of Butler.

Applicants' arguments are those made in the 102 rejection and have been addressed above under the 102 rejection heading.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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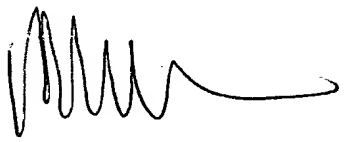
If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER